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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,937	07/17/2006	David Morton	478.1076	8966

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EXAMINER	
LEA, CHRISTOPHER RAYMOND	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,937	MORTON ET AL.	
	Examiner	Art Unit	
	Christopher R. Lea	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24,39-43,46,47,49-57 and 59-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,39-43,46,47,49-57 and 59-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 (national stage application) of PCT/GB04/03935.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 1, 2010, has been entered.

Receipt of Amendments/Remarks filed on June 1, 2010, is acknowledged. In response to Final office action dated December 31, 2009, applicant amended claim 23, canceled claim 48, and added new claim 65. Claims 23, 24, 39-43, 46, 47, 49-57, & 59-65 are pending. Claims 23, 24, 39-43, 46, 47, 49-57, & 59-65 are under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. All new rejections applied have been necessitated by applicant's amendment to the claims. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 23, 24, 39-43, 46, 47, 49-57, & 59-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating premature ejaculation with clomipramine, does not reasonably provide enablement for treatment with all antidepressants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands,* 8 USPQ2d1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure.

Scope or breadth of the claims

The claims are drawn to a method of treating premature ejaculation (PE) through the oral administration of an antidepressant. The claims encompass any antidepressant.

Nature of the Invention

The invention is a method of administering to the lungs an antidepressant to treat premature ejaculation.

Relative level of skill possessed by one of ordinary skill in the art

"A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 167 LEd2d 705, 82 USPQ2d 1385, 1397 (2007). "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id.* Office personnel may also take into account "the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* At 1396, 82 USPQ2d at 1396. The "hypothetical person having ordinary skill in the art' to which the claimed subject matter pertains would, of necessity have the capability of understanding the scientific and engineering principles applicable to the pertinent art." *Ex parte Hiyamizu*, 10 USPQ2d 1393, 1394 (Bd. Pat. App. & Inter. 1988) (The Board disagreed with the examiner's definition of one of ordinary skill in the art (a doctorate level engineer or scientist working at least 40 hours per week in semiconductor research or development), finding that the hypothetical person is not definable by way of credentials, and that the evidence in the application did not support the conclusion that such a person would require a doctorate or equivalent knowledge in science or engineering.).

State of, or the amount of knowledge in, the prior art

Bolell (US PreGrant Publication 2002/0091129) teaches that around the time of the invention, no drugs had been approved for the treatment of premature ejaculation, but that a few antidepressants (namely the tricyclic clomipramine and the SSRIs sertraline, and paroxetine) had "off-label" use as such.

Level or degree of predictability, or lack there of, in the art

The pharmaceutical arts are inherently unpredictable. There is also unpredictability in the conventional prior art methods of premature ejaculation treatment; particularly, the rational development of new PE treatments is hampered by the poor understanding of its causative mechanisms in general.

Amount of guidance or direction provided by the inventor

The application lists over 100 antidepressant compounds by name (though there are possible dozens more unnamed) that may be used in the present invention; however, the applicant cites only two independent studies that treated PE with antidepressants. These two studies used clomipramine or clomipramine, paroxetine and sertraline. Additionally, the instant specification discloses that "The mechanisms by which the various antidepressants are thought to work vary considerably between the various types of antidepressants" (page 6, lines 14-16). Hence, there is no expectation that any given antidepressant would be effective to treat PE, based solely on the fact that it functions as an antidepressant.

Presence or absence of working examples

All of the working examples disclosed by applicant make use of clomipramine.

Quantity of experimentation required to make and use the invention

The experimentation would consist of picking an antidepressant, formulating it in an inhalable composition, administering it to a subject in need of treatment, and determining whether or not it was effective for treating PE. If unsuccessful, which is likely given the few that have shown effect and the relatively large number of antidepressants, the skilled artisan would be forced to select another antidepressant

and repeat the unpredictable process again until successful. Therefore, it would require undue experimentation to use the invention in a manner commensurate in scope with the claims.

In conclusion, given the lack of working examples that incorporate an antidepressant other than clomipramine, the dearth of results for the treatment of PE by antidepressants save clomipramine, paroxetine, and sertraline, and the absence of an antidepressant being approved for the treatment of PE (at least at the time of the invention), the person of ordinary skill in the art would have to engage in an undue amount of experimentation to use the invention in a manner commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 23, 24, 39-43, 46, 47, 49-54, & 59-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tam et al. (US PreGrant Publication 2002/0161016) in view of Staniforth et al. (US PreGrant Publication 2003/0162835).

Applicant claims

Applicant claims a method for treating premature ejaculation through the pulmonary inhalation of an antidepressant in the form of a dry powder.

Determination of the scope and content of the prior art (MPEP 2141.01)

Tam et al. teach, as a whole, administration of antidepressants to treat premature ejaculation.

Claims 23, 46, 47, & 49-54: Tam et al. teach a composition containing an antidepressant, wherein the composition is administered to a subject "as needed" to treat premature ejaculation (PE) (paragraph 13, and claims 1 & 21). Tam et al. teach that the composition may be administered via inhalation (paragraph 15). Tam et al.

teach that clomipramine is the particularly preferred antidepressant (paragraph 40). Tam et al. teach that the non-aerosol compositions for inhalation may comprise a dry powder in which the powder has an average particle size of 0.1 μm to 50 μm, preferably 1 μm to 25 μm (paragraph 74).

Claim 24: As to the claimed side effect profile, where the claimed and prior art products are substantially identical in structure or composition, or are produced by substantially identical processes, a *prima facie* case of obviousness has been established. Further, The U.S. Patent Office is not equipped with analytical instruments to test prior art compositions for the infinite number of ways that a subsequent applicant may present previously unmeasured characteristics. When as here, the prior art appears to contain the exact same ingredients and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is properly shifted to applicant to show otherwise. Absent evidence to the contrary, the prior art composition must possess the claimed side effect profile, since it is substantially identical to the claimed composition (See MPEP § 2112.01).

Claim 39: Tam et al. teach that a single antidepressant or a combination of antidepressants can be administered in the composition (paragraph 44).

Claims 40-42: Tam et al. teach that other active agents (not antidepressants) can be administered in the composition (paragraphs 44-46). Tam et al. also teach that the other active agents will generally be one that is effective in treating PE (paragraph 44). Tam et al. specifically teach benzodiazepines as possible other active agents (paragraph 46).

Claims 43, 59, & 60: Tam et al. teach that the composition delivers 0.1-300 mg per dose (paragraph 78).Tam et al. teach a composition (example 5) that has an effective dose of 8.25-24.75 mg (2.5 g in 100mL, 0.33mL/compression, 1-3 compressions/dose, paragraphs 92-95).

Claims 61-65: As to the claimed onset of efficacy, where the claimed and prior art products are substantially identical in structure or composition, or are produced by substantially identical processes, a *prima facie* case of obviousness has been established. Further, The U.S. Patent Office is not equipped with analytical instruments to test prior art compositions for the infinite number of ways that a subsequent applicant may present previously unmeasured characteristics. When as here, the prior art appears to contain the exact same ingredients and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is properly shifted to applicant to show otherwise. Absent evidence to the contrary, the prior art composition must possess the claimed onset of efficacy, since it is substantially identical to the claimed composition (See MPEP § 2112.01).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the teachings of Tam et al. and the instant claims is that Tam et al. do not specifically teach the claimed size limitations, excipients, and carrier particles. This deficiency in Tam et al. is cured by the teachings of Staniforth et al.

Staniforth et al. teach, as a whole, a method for making particles suitable for use in pharmaceutical compositions (abstract).

Claims 23, 24, 39-43, 49, & 59-65: Staniforth et al. teach making composite excipient particles (particles that contain excipient and active agent) for use in formulations for the local administration of agents including antidepressants (paragraph 48). Staniforth teach that the particulate compositions are suitable for use in dry powder inhalers (paragraph 50). Staniforth et al. teach that 90% by weight of the composite excipient particles have a diameter of less than 10 μm advantageously and less than 5 μm preferably (paragraph 51).

Claims 46 & 47: Staniforth et al. teach that the composite excipient particles have a mass median aerodynamic diameter of not more than 10 μm advantageously and not more than 5 μm preferably (paragraph 51).

Claims 50 & 53: Staniforth et al. teach that the composite excipient particles comprise an excipient and an additive material (paragraph 51).

Claim 51: Staniforth et al. teach that the optimum amount of additive material will depend on chemical nature of the additive material and excipient (paragraph 24). Further, Staniforth et al. teach that additive material is preferably 2-20% based on the total weight of the additive material and excipient (paragraph 24). Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation (MPEP § 2144.05).

Claim 52: Staniforth et al. teach that leucine, magnesium stearate, lecithin, and sodium stearyl fumarate may be additive materials (paragraphs 33-36).

Claim 54: Staniforth et al. teach the inclusion of carrier particles in the composition (paragraph 54) and that the particles are of the size between 20 and 250 μm preferably (paragraph 55).

Finding of *prima facie* obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the methods for making an inhalable pharmaceutical taught by Staniforth et al. to formulate a composition for use in the method taught by Tam et al. and produce the instant invention. The skilled artisan would have been motivated to combine the teaching of the references because it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, namely for inhalation administration of an antidepressant, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (See In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) and MPEP § 2144.06).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in using the methods for making an inhalable pharmaceutical taught by Staniforth et al. to formulate a composition for use in the method taught by Tam et al. and producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

7. Claims 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tam et al. and Staniforth et al. as applied to claim 23 above, and further in view of Lewis et al. (US PreGrant Publication 2002/0025299).

Applicant claims

Applicant claims a method for treating premature ejaculation through the pulmonary inhalation of clomipramine in a form useful in a pressurized metered dose inhaler.

Determination of the scope and content of the prior art (MPEP 2141.01)

Detailed discussion of the rejection of claim 23 and the teachings of Tam et al. and Staniforth et al. appears above.

Claims 55-57: Tam et al. teach that the formulations for inhalation may be in the form of aqueous solutions and/or suspensions (paragraph 74).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the teachings of Tam et al. and the instant claims is that Tam et al. do not teach using the composition in a pressurized metered dose inhaler. This deficiency in Tam et al. is cured by the teachings of Lewis et al.

Lewis et al. teach, as a whole, stable pharmaceutical compositions for administration in a pressurized metered dose inhaler. Lewis et al. teach that the

compositions may be used to administer active agents besides those specifically disclosed (paragraph 24).

Claim 55: Lewis et al. teach a composition comprising a solution of co-solvent and propellant in a pMDI (paragraph 16).

Claim 56: Lewis et al. teach that formulations for use in a pMDI can be a suspension, though this has been problematic (paragraph 4)

Claim 57: Lewis et al. teach that the propellants for use in the composition are HFAs, specifically HFA 134a and HFA 227 (paragraph 8).

Finding of *prima facie* obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the composition useful as an inhalable pharmaceutical taught by Lewis et al. to formulate a composition for use in the method taught by Tam et al. and produce the instant invention. The skilled artisan would have been motivated to combine the teaching of the references because it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, namely for inhalation administration of an active agent, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (See In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) and MPEP § 2144.06).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in using the composition useful as an inhalable pharmaceutical taught by Lewis et al. to formulate a composition for use in the method taught by Tam et al. and producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

In light of the forgoing discussion, one of ordinary skill in the art would have concluded that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Response to Arguments

8. Applicant's arguments filed June 1, 2010, have been fully considered but they are not persuasive.

Applicant argues that "[T]here is no teaching of suggestion provided by the Tam reference to use a dry powder as claimed for pulmonary inhalation." This assertion is clearly false. Reproduced below is the final portion of paragraph 74 from the Tam reference with emphasis added by the examiner:

> Non-aerosol formulations **for inhalation** may also comprise **dry powder formulations**, particularly insufflations in which the powder has an average particle size of about 0.1 μm to 50 μm, preferably 1 μm to about 25 μm.

This definitively shows that Tam et al. teach and suggests dry powder of pulmonary inhalation (insufflation). Applicant's argument that Tam et al. teach away from dry

powder inhalation is clearly also defective. Applicant's arguments are also undermined with their references to column and line numbers, whereas the reference is divided into paragraphs. As such the sections referenced by applicant (e.g. col. 9, l. 48-50) are not able to be located in the reference.

Applicant argues that "the Staniforth reference does not disclose a dry powder wherein 90% of the antidepressant has a MMAD particle size of 10μm or less." While the Staniforth reference may not disclose such an embodiment, it certainly teaches and/or suggests one. As applicant has admitted, Staniforth et al. teaches that 90% of the composite excipient particles may have a diameter less than 10 μm and that the composite excipient particles are particles that contain excipient and active agent, which may include antidepressants. Therefore, Staniforth et al. clearly teach and/or suggest a powder comprising an antidepressant (that it also includes excipient is not precluded by the claims) of which 90% by weight has MMAD less than 10μm. Applicant's argument that Staniforth et al cannot be combined with Tam et al. is based on the previously rebutted premise that Tam et al. teach away from dry powder inhalation.

Applicant's arguments against Lewis are moot in view of the newly applied grounds of rejection necessitated by applicant's amendment to claim 23.

The expected result remains the same; an inhalable powder comprising an antidepressant for treating premature ejaculation is made in the absence of evidence to the contrary. No unexpected results have been presented. Applicant's arguments are not persuasive, and the rejection under 35 U.S.C. §103(a) is maintained.

Conclusion

Claims 23, 24, 39-43, 46, 47, 49-57, & 59-65 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Lea whose telephone number is (571) 270-5870. The examiner can normally be reached on Mon-Fri 7:30-3:30 ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne "Bonnie" Eyler can be reached on (571)272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/C. R. L./
Examiner, Art Unit 1619

crl

/Ernst V Arnold/
Primary Examiner, Art Unit 1616